

(19)



Europäisches Patentamt
European Patent Office
Office européen des brevets



(11)

EP 0 865 763 B1

(12)

EUROPEAN PATENT SPECIFICATION

(45) Date of publication and mention
of the grant of the patent:
24.04.2002 Bulletin 2002/17

(51) Int Cl.7: **A61B 5/05**

(21) Application number: **98500063.7**

(22) Date of filing: **04.03.1998**

(54) **Apparatus for measuring volumes and global and segmental corporal composition in human beings**

Vorrichtung zur Messung des Volumens und der ganzheitlichen und abschnittsweisen
Zusammensetzung des menschlichen Körpers

Dispositif de mesure du volume et de la composition globale et segmentaire du corps humain

(84) Designated Contracting States:
DE DK FR GB IT

(30) Priority: **06.03.1997 ES 9700499**

(43) Date of publication of application:
23.09.1998 Bulletin 1998/39

(73) Proprietor: **NTE, S.A.**
08186 Lliça d'Amunt (Barcelona) (ES)

(72) Inventors:
• **Rosell Ferrer, Javier**
08071 Barcelona (ES)
• **Elvira Canas, Jordi**
08014 Barcelona (ES)

- **Riu Costa, Pere**
08071 Barcelona (ES)
- **Bragos Bardia, Ramon**
08071 Barcelona (ES)
- **Pallas Areny, Ramon**
08071 Barcelona (ES)

(74) Representative: **Davila Baz, Angel**
c/o Clarke, Modet & Co.,
Goya, 11
28001 Madrid (ES)

(56) References cited:
US-A- 5 335 667 **US-A- 5 579 782**

EP 0 865 763 B1

Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

Description

[0001] The present invention refers to an apparatus and a procedure for measuring volumes and global and segmental corporal composition, such as the ratio between intracellular and extracellular water, as well as the ratio between lean mass and fatty mass in human beings.

[0002] The measuring equipments currently in existence in the Market, do not offer regional or segmental measurements of the human body, thus enormously limiting the information obtained.

[0003] Spanish Patent Application ES 9300378 describes a procedure for the determination of the composition of substances of fleshy nature by means of impedance measurements, but which only uses two measurements determining from them, a value related to the ratio between intracellular water and extracellular water and in consequence, the errors obtained are great. Additionally, said procedure is not capable of extracting any information on the composition of fat in the flesh studied.

[0004] US-A-5,335,667 discloses a method and apparatus for determining body composition using bioelectrical impedance. The method is based on the selection of a number of body segments having an uniform cross-sectional area, the injection of a single high-frequency low level of current into the body bilaterally using four electrodes simultaneously attached to the subject, and the measurement of the impedance at said single frequency of each body segments.

[0005] US-A-5,579,792 discloses a portable device and a method for measuring the amount of fat in a body. The method is based on a separate estimation of the subcutaneous and the visceral fat by measurements of the body impedance upon injecting alternately and separately two different constant current high-frequency signals.

[0006] A multitude of equations exist which relate the volume content and the corporal composition, all of which introduce errors which may become important and prevent the measurement of significant changes in the body, both in volume and in composition, if used with a very reduced number of experimental data, as happens in the procedure described in document ES 9300378.

[0007] Consequently, the object of the present invention is to provide a procedure and a measuring apparatus which determine in a more reliable manner, the global and segmental corporal composition, especially the ratios between the volumes of intracellular water and extracellular water, as well as the ratio between fatty mass and lean mass of the body under research.

[0008] This task is solved by means of the procedure and the apparatus of the present invention, which permits the measurement of the volume and the corporal composition, both globally and segmentally, by means of a series of measurements of the electrical impedance at various frequencies, at least four, in the range of 1

kHz to 1 MHz. With the values obtained, first a parameter K is calculated, given by the quotient between the impedance module Z(BF) at a low frequency, between 1 kHz and 50 kHz, and the impedance module Z(AF) at a frequency between 100 kHz and 1 MHz, which serves as an estimation of the ratio between the volumes of intracellular water and extracellular water. This value is independent from the contour conditions of the measurement. The experimental values are herewith adjusted, both at global level and at segmental level with the function:

$$Z(f) = R_{\infty} + \frac{R_0 - R_{\infty}}{1 - \left(\frac{f}{f_c}\right)^{1-\alpha}}$$

by means of the least squares from which the adjustment parameters R_{∞} , R_0 , f_c and α are determined, which represent the resistance at infinite frequency, the resistance at zero frequency, the frequency at which the maximum of $\text{Im}(Z)$ occurs and the dispersion of the cells size of the biological system, respectively. Parting from these adjustment parameters the following values are calculated:

a) E, defined by :

$$E(\%) = \frac{R_0 - R_{\infty}}{R_{\infty}}$$

which reflects the ratio between the volumes of intracellular water and extracellular water;

b) the total water content of a segment i ($TBW_{\text{seg},i}$), given by:

$$TBW_{\text{seg},i} = ko_{TBW_{\text{seg},i}} + \frac{K_{TBW} \cdot H^2 \cdot L_{\text{seg},i}^2}{\text{Real}[Z(\infty)]}$$

and the content of a segment i in extracellular water ($ECW_{\text{seg},i}$) which is determined by:

$$ECW_{\text{seg},i} = ko_{ECW_{\text{seg},i}} + \frac{K_{ECW} \cdot H^2 \cdot L_{\text{seg},i}^2}{\text{real}[Z(10\text{KHz})]}$$

h being the height of the body in cm, K_{TBW} a proportionality constant for the total water (TBW) and K_{ECW} proportionality constant for the extracellular water, $ko_{TBW_{\text{seg},i}}$ the independent term of segment i, $ko_{ECW_{\text{seg},i}}$ is for extracellular water (ECW) for segment i, $L_{\text{seg},i}$ and $L'_{\text{seg},i}$ geometric terms to be determined for each segment; corresponding the real value $[Z(\infty)]$ at the real value of an impedance over 100 kHz and less at 1 MHz for segment i, but pref-

erably at R_∞ , and the real value $[Z(10 \text{ kHz})]$ at the real value of an impedance over 10 kHz and below 50 kHz for segment i, but preferably at R_0 ;

[0009] The obtention of the coefficients is conducted as follows:

- 1.- having a statistically significant sample of subjects, the volumes of the total and the global and segmental extracellular water are measured by means of different methods to those presented in this patent.
- 2.- adjusting by lineal regression of least squares between the total and extracellular global volumes and the ratios:

$$\frac{H^2}{Re[Z(0)]}$$

and

$$\frac{H^2}{Re[Z(\infty)]}$$

- respectively, (where Z is the right side impedance, that is to say, that of the right arm and leg plus that of the trunk measure in series at one time) slopes K_{ECW} and K_{TBW} are respectively obtained.
- 3.- adjusting by lineal regression of the least squares among the ratio:

$$\frac{H^2 \cdot K_{TBW}}{Re[Z(\infty)]}$$

(where Z is segmental) and the segmental total water measured, a slope $L_{seg,1}^2$ is obtained for each i segment, and an independent term $ko_{TBW,seg i}$ for each segment.

- 4.- adjusting by lineal regression of least squares between the ratio:

$$\frac{L_{seg,i}^2 \cdot H^2 \cdot K_{ECW}}{Re[Z(0)]}$$

(where Z is segmental) and the segmental extracellular water measured with another method, a slope ψ_i is obtained for each segment and an independent term $ko_{ECW,seg i}$ for each segment i.

- 5.- next an extracellular water formula $L_{seg,1}^2$ is replaced by

$$L_{seg,i}^2 = \psi_i \cdot L_{seg,i}^2$$

$L_{seg,i}^2$ and $L_{seg,i}$ include geometric information with- in the determination formulas of volumes.

- c) the contents of segment i in intracellular water which is determined by means of the subtraction of $ECW_{seg,i}$ from $TBW_{seg,i}$

- d) of the total and extracellular water at global level which is determined by the sum of the respective values of segments i

- e) the segmental or regional lean mass content $MM_{seg,1}$ and the global by means of equation.

$$MM_{seg,i} = \text{Lean Mass} = N + M \frac{D_{eq}^2 \text{ seg.i}}{R(AF)}$$

N and M being terms which are introduced from the lineal regression between relation

$$\frac{D_{eq}^2 \text{ , seg.i}}{Re[Z(\infty)]}$$

and the average lean mass value by means of an alternative method and which shall depend on the type of human race, and $D_{eq,seg,i}^2$ a geometric parameter of segment i, obtaining the global value of the amount of lean mass and the sum of all the $MM_{seg,i}$ values and the global fatty mass of the difference between the weight of the human body studied and the weight of the amount of global lean matter.

[0010] Additionally the task of this invention is solved because the previously described procedure is conducted by means of a measuring apparatus which consists of a rear connection board (backplane) which interconnects four boards and an electric source, said boards consisting of a signal generator board which generates two or more selectable frequencies as well as reference signals for the demodulation, in an interface board with the user who converts the tension signals generated into current, into a board for signal detection (signal detection board) which is made up of a differential amplifier and a gain amplifier with selectable gain by means of software, into an A/D obtention board which is provided with a A/D converter of preferably 16 bits for sampling for data obtention.

[0011] The electrical source is connected to the body under study by means of a multiplexor which permits any electrode couple to be connected to the said source, connecting each one of the electrodes to an in-put buffer whilst each one of their out-puts is connected to a multiplexor circuit. This multiplexor feeds a differential amplifier, by means of shielded coaxial cables. The control of the system is conducted by means of a microcontrol-

ler.

[0012] The procedure and the apparatus of the present invention is herewith described by means of an embodiment example, with the help of the drawings in which:

Figure 1 shows a spectrum of the electrical impedance module based on frequency f ;

Figure 2 shows a schematic diagram of connections corresponding to the electrical constellation of a body.

Figure 3 shows two spectra of the complex impedance based on the frequency.

Figure 4 shows an embodiment example of the measuring apparatus according to the invention.

Figure 5 shows the block diagram of the apparatus of figure 4.

Figure 6 shows the interconnections between the diverse boards, and

Figure 7 shows the zones of the body in which the electrodes are placed.

[0013] The apparatus and the procedure, which are the object of the invention, are based on the study of a physical phenomenon which is denominated relaxation in the electrical impedance signal. This phenomenon is explained in total detail by K. Forster and H. Schwan, "Dielectric Properties of Tissues and Biological Materials: A Crucial Review" in Critical Reviews in Biomedical Engineering, volume 17, part 1 (1989). This relaxation consist of a fall in the electrical impedance value with the electrical signal frequency used to measure the same in any medium whatsoever. The electrical impedance of a medium is broken up into a real part and another imaginary part. The real part is what is commonly known as electric resistance and the imaginary part, in the case of biological tissues, corresponds to the electric capacity of the medium in question. The relaxation phenomenon has its explanation in the absorption of electromagnetic energy. A simple electric model is accepted by conviction where the capacitance character of the cellular membrane produces said absorption of energy (figure 2). The resistance of the extracellular medium is modelled by a R_e resistance and the intracellular medium resistance is modelled by another R_i resistance. The capacity of the cellular membrane is modelled by a C capacitor. When the Z electric impedance is measured based on the f frequency in a circuit such as the one presented in figure 2, a graph is obtained such as the one presented in figure 1. If the injected signal is of high frequency, an electric impedance is obtained which is equal to the parallel of the two resistances of the circuit and if it is of low frequency, it is equal to the extracellular R_e resistance.

[0014] The frequency at which the fall of the impedance is presented depends on the type of cell as an average of the measured biological system. The animal cells, for example, have a relaxation frequency below

that of bacteria. In consequence, the measurement of the electric impedance at various frequencies by the apparatus of the present invention permits a determination of the type of average cell existing in the human body or region of the latter which is being measured.

[0015] Figure 3 presents a form of representing the impedance of a biological system (a curve corresponds to a segment and the other to the impedance of the right hand side), that is to say, the imaginary part of the impedance based on the real part. In said drawing, the impedance of a biological system can be seen to draw a flat half-circumference. This graph is well known and is denominated Cole-cole graph. The cut frequency may be seen as the point where the complex part of the impedance presents the highest value. The flattening of the half-circumference is related to a parameter called α . Other two parameters are R_0 and R_∞ and obtains the value of the real part of the impedance in direct current and at very high frequency (over 1 MHz) by means of the extrapolation of the adjustment without requiring to measure it. That is to say, four parameters are available which describe the human body or region of the latter which is measured: resistance in direct current R_0 , resistance at very high frequency R_∞ , cut frequency F_c and flattening value of the half-circumference α .

[0016] In the procedure of the present invention, the composition of the researched body is obtained, parting from said 4 parameters.

1) Measurement of the electrical impedance with a frequency scan of 1 kHz at 10 MHz to obtain the graph of figure 1. Four measuring points in the said range is the minimum number of measurements required for reproducing the curves of figures 1 and 3. The measurement is conducted by injecting an electric current of determined frequency through two electrodes connected to the skin and measuring the fall of the current tension applied through the other two electrodes, also connected to the skin. This is the base of the impedance measurement at four wires which is very resistant to the influence of the electrode impedance. This measurement of impedance is conducted with currents of various frequencies until a minimum of 4 points of frequency are obtained in the range of 1 kHz to 1 MHz and this is repeated for each segment i .

2) On the body, 11 electrodes may be placed with the apparatus which is the object of the invention. Grouping said electrodes in 4's, up to 7 segments or human regions are obtained. The distribution of regions which are given in default in the measuring apparatus is the result of placing the 11 electrodes according to figure 7. This placement of electrodes permits the measurement of the impedance at various frequencies according to the process of point 1 for the following segments: head and neck, right arm, left arm, thorax, abdomen, right leg and left leg. Other distributions of regions is possible and it only

requires the distribution in 4's of the 11 electrodes until 7 segments are made. The measuring apparatus permits the selection of injecting electrodes and tensiometers. This permits any type of electrode to be injector or measurer.

3) Obtention of an assembly of experimental data on electrical impedance at frequencies of 1 kHz to 1 MHz, regional and global of the human body.

[0017] Parting from this point, the procedure, according to the present invention, processes this assembly of data in different ways to obtain a set of information which will permit to know the volumes and corporal composition of the human body measured.

[0018] The first stage of the procedure is the obtention of parameter K. It is a first simple calculation to be conducted by the measurer to permit the ratio between the total water and the extracellular water volumes in the body being studied and is conducted as follows:

1) K is obtained by the quotient of an impedance value at low frequency (between 1 kHz and 50 kHz) and one at high frequency (over 100 kHz up to 1 MHz) :

$$K = \frac{|Z(BF)|}{|Z(AF)|}$$

where $|Z(AF)|$ and $|Z(BF)|$ are the values of the module of the electrical impedance at high and low frequency respectively

2) This ratio is associated to the ratio of volumes of the extracellular water of the total water of the body. This ratio is conducted both at global and at segmental level.

[0019] The second stage corresponds to a more complete study of the obtained data. This study consists of the adjustment of the Cole-cole model to the data by means of the following steps:

1) The electrical impedance measurements resulting from the scanning in frequency (at least four measurements of 1 kHz to 1 MHz) and at global and segmental level are adjusted by the function:

$$Z(f) = R_{\infty} + \frac{R_0 - R_{\infty}}{1 + \left(\frac{f}{f_c}\right)^{1-\alpha}}$$

by means of an adjustment of least squares. This function simulates the dependence of the electrical impedance (Z) as regards frequency f. The adjustment parameters R_0 and R_{∞} are the resistances which present the medium in direct current and at very high frequency respectively, f_c is the frequency at which the maximum of the imaginary part is pro-

duced and depends on the type of cell measured in the biological system; and α is a parameter which is related to the dispersion of dimensions of the cells of the measured biological system. The expression of this point 1 reproduces the curve of figure 3 which would be obtained if a great amount of points were measured.

2) Parting from the first two adjustment parameters found (R_0 and R_{∞}) we obtain a value called E which gives the relation between the intracellular water and the extracellular water volumes:

$$E(\%) = \frac{R_0 - R_{\infty}}{R_{\infty}} \quad 15$$

The impedance measured may be modelled as the previously described circuit which is presented in figure 2. The ratios between the parameters of circuit (R_e and R_i) with that of the mathematical model are as follows:

$$R_e = R_0$$

$$R_i = \frac{R_0 \cdot R_{\infty}}{R_0 - R_{\infty}} \quad 25$$

3) The series of parameters obtained from the adjustment are associated to characteristics of composition of the body at global and segmental level:

- a) Ratios of E, which give an idea of the ratio between volumes of extracellular and intracellular water.
- b) Cut frequency (f_c), and
- c) flattening of the curve presented in figure 3 (α).

[0020] The third stage will offer information on the corporal volumes and will permit the studying of its changes. This procedure uses the impedance at 10 KHz and at a greater frequency than 100 kHz or else parameters R_0 and R_{∞} obtained by the previous stage. The steps to be followed are :

1) The necessary values are parameters R_0 and R_{∞} . These parameters are introduced in the following formulas to determine the volume of total water and extracellular water:

$$TBW_{seg,i} = k^{O_{TBWseg,i}} + \frac{K_{TBW} \cdot H^2 \cdot L_{seg,i}^2}{real[Z(\infty)]}$$

$$ECW_{seg,i} = ko_{ECWseg,i} + \frac{K_{ECW} H^2 \cdot L_{seg,i}^2}{Re[Z(10kHz)]} \quad 20$$

where $TBW_{seg,i}$ is the content of segment i in total water and $ECW_{seg,i}$ the content of segment i in extracellular water, H is the height of the body in cm, K_{TBW} is proportionality constant for the total water (TBW) and K_{ECW} for the extracellular water, $ko_{TBWseg,i}$ is the independent term for the total water equation (TBW) of segment i , and $ko_{ECWseg,i}$ for the extracellular water (ECW) of segment i . $L_{seg,i}$ and $L'_{seg,i}$ are geometric terms to be determined for each segment i . The obtention of the coefficients is conducted in the following manner:

a) with a statistically significant sample of subjects, the volumes of total and global and segmental extracellular water are measured by means of methods other than those which are presented in this Patent.

b) Adjusting by lineal regression of least squares between the total and extracellular global volumes and the ratios:

$$\frac{H^2}{Re[Z(0)]}$$

and

$$\frac{H^2}{Re[Z(\infty)]}$$

respectively, where Z is the right hand side impedance, that is to say, that of the right arm and leg plus that of the trunk, the slopes K_{ECW} and K_{TBW} are respectively obtained.

c) adjusting by lineal regression of the least squares between the ratios;

$$\frac{H^2 \cdot K_{TBW}}{Re[R(\infty)]} \quad 20$$

(where Z is segmental) and the segmental total water measured, a slope $L_{seg,i}^2$ is obtained for each segment i and an independent term $ko_{TBWseg,i}$ for each segment i

d) adjusting by lineal regression of the least squares between the ratios:

$$\frac{L_{seg,i}^2 \cdot H^2 \cdot K_{ECW}}{Re[Z(0)]} \quad 55$$

(where Z is segmental) and the segmental ex-

tracellular water measured by means of another method, a slope ψ_i is obtained for each segment i and an independent term $ko_{ECWseg,i}$ for each segment i .

e) a change is conducted on formula $L_{seg,i}^2$ of extracellular water by

$$L_{seg,i}'^2 = \psi_i \cdot L_{seg,i}^2$$

$L_{seg,i}'^2$ and $L_{seg,i}$ include geometric information within the formulas for volume determination.

These equations provide the value of the total water and of the extracellular water for segment i . The real value $[Z(\infty)]$ corresponds to R_{∞} or to the real value of an impedance over 100 kHz and below 1 MHz for segment i ; and the real value $[Z(10kHz)]$ corresponds to R_0 or to the real value of a superior impedance at 10 kHz and below 50 kHz for segment i .

Parameters K_{TBW} , K_{ECW} , $ko_{seg,i}$, $ko_{seg,i}'$ depend on the race the human body belongs to and are adjusted by means of calibration. Values $ko_{seg,i}$, $ko_{seg,i}'$ additionally depend on the segment in question. Values L_{eq} and L_{eq}' provide geometric information of the segment in question.

2) The values of the total water and of the extracellular water are obtained according to the given formulas. The segments in question may be, for example; head and neck, thorax, abdomen, legs and arms, and are obtained with the distribution of electrodes (0 to 10) of figure 7. For other segments, new values of $ko_{seg,i}$, $ko_{seg,i}'$ and L_{eq} shall be adjusted. The values of the intracellular water volume is obtained from the subtraction of the volume of extracellular water of the total water volume.

3) The value of the volume of total and extracellular water for all the body, that is to say, at global level, is calculated as the sum of all the segments i mentioned in point 4 (for example, head and neck, right leg, left leg, thorax, abdomen, right arm and left arm). The global values may also be obtained using the RSI (Right Side Impedance (impedance of the right side) which is constituted by the right leg and arm plus trunk, as if it were a segment, conveniently considering the specific parameters of the formula for this segment. Said impedance of the right side is extensively described in: Kushner R.F., and Schoeller D.A., "Estimation of Total Body Water by Bioelectrical Impedance Analysis", Am.. J.Clin. Nutr. 44, 417-424 (1986). The global value of the intracellular water volume is obtained by the subtraction of the extracellular water volume from the total water volume.

[0021] The global values of the water volume calculated according to the third stage produce according to the same, much more exact values than those using the

RSI according to the formulas in compliance with the state of the art.

[0022] The fourth stage to be conducted provides information on the content of the lean mass both segmental and global. Said stage follows the next steps:

- 1) Using the resistance value at high frequency (equal or over 100 kHz) for the obtention of the amount of fat which is presented according to the following expression:

$$MM_{seg,i} = \text{Lean Mass} = N + M \cdot \frac{D_{eq,seg,i}^2}{Re[Z(\infty)]}$$

30

N and M being terms which are introduced from the lineal regression between the ratio.

$$\frac{L_{eq,seg,i}^2}{Re[Z(\infty)]}$$

and the value of lean mass measured by means of an alternative method and which depends on the type of human race, and $D_{eq,seg,i}^2$, a geometric parameter of segment i, obtaining the global value of the amount of lean mass from the sum of all the $MM_{seg,i}$ and the amount of global fatty mass of the difference between the weight of the human body studied and the weight of the amount of global lean matter.

2) The value of the amount of global lean matter of the body shall be obtained from the sum of all the amount of segmental or regional lean matter.

3) The value of the amount of global fat shall be obtained by subtracting from the weight of the human body studied, the amount of global lean matter obtained by the sum of all the amount of segmental lean matter.

[0023] All the stages may also be used for measuring the quantity of segmental lean matter from any region which is defined outside those previously indicated (head and neck, right leg, left leg, right arm, left arm, thorax and abdomen). Using only two pairs of electrodes from the system, any anatomical region of measurement may be defined.

[0024] These four stages use the electrical impedance values, both real part and imaginary part, measured within a frequency range between 1 kHz and 1 MHz.

[0025] The apparatus which is also the object of this invention, is a measuring apparatus of electrical impedance at various frequencies. This impedance measuring apparatus measures both the real part and the imaginary part at eight frequencies selected by the user. These

eight frequencies may go from 1 kHz to 1 MHz. The measuring apparatus is made up of a computer (11) which controls an electronic box (12), fed through the feeding source (14) coming out from said electronic box (12), in a preferred manner, eleven electrodes (13) which are placed, for example, as shown in figure 7. Figure 4 presents the concept of the system.

[0026] As may be observed in figure 7, four electrodes (2, 3, 9, 10) are placed at the ends of the forearm, four at the ends of the legs (5, 6, 7, 8), two (0, 1) on the forehead and one (4) on the point of the breastbone. These electrodes are used as injectors and/or detectors for measuring all the segments which make up the body and which have been previously indicated. Other combinations of electrodes may be chosen to create other regions which shall not necessarily be such, that will give, after summing them up, the totality of the human body.

[0027] The measuring apparatus which is the object of the present invention, is designed according to a block diagram such as the one presented in figure 5. The apparatus is formed by a rear connection board, (backplane) (15) which interconnects four boards (16, 17, 18, 19) and an electric source (20). The board (16) of the generator for the signal (signal generator) generates two selected frequencies and reference signals for demodulation. The board (17) for interface with the user (patient interface) converts the generated tension signals into current, the board (18) for detection of the signal is made up of a differential amplifier and gain amplifier with selected gains via software. Then, the signal is demodulated, using four analogical multipliers and four integrators, the board (19) for A/D obtention is provided with an A/D convertor of preferably 16 bits for sampling, for the obtention of data. The control of the system is conducted by a microcontroller. The microcontroller sends orders to the other boards of the system.

[0028] The electrical source (20) is connected to the body under study through a multiplexor which permits any pair of electrodes to connect to the said source. Each one of the eleven electrodes (0 to 10) are connected to an in-put buffer using shielded coaxial cables (21). Each out-put of the buffer is connected to a multiplexor circuit which feeds a differential amplifier. Five buffers are available plus those to which internal calibration impedances are connected.

[0029] The interconnections between the board (19) for A/D obtention, the board (18) for signal detection, the board (16) of the signal generator and the front end (17) are presented in figure 6.

[0030] With this measurer and the procedure previously presented, a highly reliable tool is available for the measurement of the amount of fluids and corporal composition.

[0031] Adding an accelerometer to this measurer which is the object of the invention, another additional application may be conducted for the use of the electrical impedance to various frequencies for the follow-up

of fluid displacement in the human body. This application consists of the follow-up of corporal fluid displacements in a human being when subjected to different accelerations other than those accelerations produced by the terrestrial gravitational fields. In consequence, the following measuring apparatus is proposed as additional object of the invention. This system consists of an apparatus such as the one previously presented with an incorporated accelerometer. The electrical impedance and the acceleration measurements are synchronized. The electrodes may be reduced in this case to those which offer the following segments: head and neck, right or left leg, right or left arm, thorax and abdomen. The electrodes are reduced in the latter case to 7 which is according to the numbering of figure 7: (0, 1, 4, 2) and (3) (or 9 and 10), (5) and (6) (or 7 and 8). The reduction of electrodes may be assumed considering that the changes shall be symmetrical in the human body under study.

[0032] This latter apparatus, fruit of the extension of the first presented, is a tool of great utility for the follow-up of the movement of fluids between the corporal regions during centrifuge pilot training and during military flights, for the control of anti-g suits.

Claims

1. Procedure for the measuring of volumes and global and segmental corporal composition in human beings, by means of measuring the electrical impedance at various frequencies, at least four, in the range comprised between 1 kHz to 1 MHz, in which a first estimation is conducted of the ratio between the total water and the extracellular water volumes by means of the k quotient between the impedance module at low frequency $Z(BF)$, placed between 1 kHz and 50 kHz, and the impedance module at high frequency $Z(AF)$, placed between 100 kHz to 10 MHz, said value k being independent from the conditions of the measurement contour, **characterized in that** an adjustment is made at the experimental points by means of the least squares method, both at global and segmental level, by means of the following electrical impedance expression (Z) based on the frequency (f);

$$Z(f) = R_{\infty} + \frac{R_0 - R_{\infty}}{1 - \left(\frac{f}{f_c}\right)^{1-\alpha}} \quad 25$$

thus determining the values R_{∞} , R_0 , f_c and α , which present the resistance at infinite frequency, the resistance at zero frequency, the frequency at which the maximum of $\text{Im}(Z)$ occurs and the dispersion of the cells of the biological system, respectively, with which the the following values are calculated:

- a) the ratio between the intracellular water and the extracellular water volumes, given by;

$$E = \frac{R_0 - R_{\infty}}{R_{\infty}}$$

- b) the total water content of a segment i ($TBW_{\text{seg},i}$), given by:

$$TBW_{\text{seg},i} = k_{TBW_{\text{seg},i}} + \frac{K_{TBW} \cdot H^2 \cdot L_{\text{seg},i}^2}{\text{Real}[Z(\infty)]}$$

- and the content of a segment i in extracellular water ($ECW_{\text{seg},i}$) which is determined by:

$$ECW_{\text{seg},i} = k_{ECW_{\text{seg},i}} + \frac{K_{ECW} \cdot H^2 \cdot L_{\text{seg},i}^2}{\text{real}[Z(10\text{KHz})]}$$

H being the height of the body in cm, K_{TBW} a constant of proportionality for the total water (TBW) and K_{ECW} a constant of proportionality for the extracellular water, $k_{TBW_{\text{seg},i}}$ the independent term for segment i, $k_{ECW_{\text{seg},i}}$ for the extracellular water (ECW) for segment i, $L_{\text{seg},i}$ and $L'_{\text{seg},i}$ are geometric terms to be determined for each segment i; corresponding the real value $[Z(\infty)]$ to the real value of an impedance over 100 kHz. and below 1 MHz for segment i, but preferably at R_{∞} , and the real value $[Z(10\text{KHz})]$ the real value of an impedance over 10 kHz and below 50 kHz for segment i but preferably at R_0 ;

- c) the content of segment i in intracellular water which is determined by means of the subtraction of $ECW_{\text{seg},i}$ from $TBW_{\text{seg},i}$.

- d) the volume of total and extracellular water at global level which shall be determined by the sum of the respective values of segments i

- e) the content of the segmental or regional $MM_{\text{seg},i}$ and global lean mass by means of the equation

$$MM_{\text{seg},i} = \text{Lean Mass} = N + M \cdot \frac{D_{\text{eq},\text{seg},i}^2}{R(AF)}$$

N and M being terms which are introduced from the lineal regression between the ratio:

$$\frac{D_{\text{seg},i}^2}{\text{Re}[Z(\infty)]} \quad 10$$

and the value of the amount of lean mass measured by means of an alternative method and

which depend on the type of human race, and $D_{eq,seg,i}^2$, a geometric parameter of segment i, obtaining the global value of the amount of lean mass from the sum of all the values $MM_{seg,i}$ and the global fatty mass from the difference between the weight of the human body studied and the weight of the amount of global lean matter.

2. Procedure according to claim 1, **characterized in that** the volumen of total and extracellular water at global level is determined using the RSI (right side impedance) as if it were a segment conveniently considering the specific parameters of the TBW and ECW formulas.
3. Apparatus for measuring the electrical impedance at various frequencies for the embodiment of the procedure according to the previous claims, **characterized in that** it consists of a backplane (15) which interconnects: an electrical source (20); a signal generator board (16) which generates at least two frequencies selected as well as reference signals for the demodulation; a board for patient interface (17) which converts the tension signals generated into current, a detection signal board (18) which is made up of a differential amplifier and a gain amplifier with selectable gains via software; an A/D obtention board (19) which is provided with an A/D convertor of 16 bits for sampling for data obtention; the current source (20) being connected to the body under study by means of a multiplexor which permits any pair of electrodes to be connected to the said source, connecting each one of the electrodes to an in-put buffer, whilst each one of their out-puts is connected to a multiplexor circuit which feeds a differential amplifier, by means of shielded coaxial cables; conducting the control of the system by means of a microcontroller.
4. Apparatus according to claim 3, **characterized in that** it is provided with an accelerometer which provides the acceleration measurement to which the body has been subjected to, in a synchronized manner with the impedance measure.

Patentansprüche

1. Verfahren zum Messen von Volumen und von globaler und segmentförmiger, körperlicher Zusammensetzung in menschlichen Wesen, durch Messung der elektrischen Impedanz bei verschiedenen Frequenzen, mindestens vier, in dem Bereich, der zwischen 1 kHz und 1 MHz liegt, indem eine erste Schätzung des Verhältnisses zwischen dem gesamten Wasservolumen und dem extrazellulären Wasservolumen, mittels des k-Quotienten zwi-

schen dem Impedanzmodul bei niedriger Frequenz $Z(BF)$, die zwischen 1 kHz und 50 kHz festgelegt ist, und dem Impedanzmodul bei hoher Frequenz $Z(AF)$, die zwischen 100 kHz bis 10 MHz festgelegt ist, durchgeführt wird, wobei der k-Wert unabhängig von den Bedingungen der Messungsoberfläche ist, **dadurch gekennzeichnet, dass** bei den Experimentierpunkten, mittels der Methode der kleinsten Quadratabweichung, eine Anpassung, sowohl für den Gesamtbereich als auch für den Segmentbereich, mittels der folgenden elektrischen Impedanzfunktion (Z) basierend auf der Frequenz (f) durchgeführt wird;

$$Z(f) = R_{\infty} + \frac{R_0 - R_{\infty}}{1 - \left(\frac{f}{f_c}\right)^{1-\alpha}}$$

wobei auf diese Weise die Werte R_{∞} , R_0 , f_c und α bestimmt werden, die den Widerstand bei unendlicher Frequenz, den Widerstand gegen Null Frequenz, die Frequenz, bei der das Maximum von $\text{Im}(Z)$ eintritt, und die Streuung der Zellen des biologischen Systems darstellen, beziehungsweise, mit denen die folgenden Werte berechnet werden:

a) das Verhältnis zwischen den intrazellulären und den extrazellulären Wasservolumen, gegeben durch:

$$E = \frac{R_0 - R_{\infty}}{R_{\infty}}$$

b) der gesamte Wassergehalt eines Segmentes i ($TBW_{seg,i}$), gegeben durch:

$$TBW_{seg,i} = k_{O_{TBW_{seg,i}}} + \frac{K_{TBW} \cdot H^2 \cdot L_{seg,i}^2}{\text{Real}[Z(\infty)]}$$

und der Gehalt eines Segmentes i an extrazellulärem Wasser ($ECW_{seg,i}$), das bestimmt ist durch:

$$ECW_{seg,i} = k_{O_{ECW_{seg,i}}} + \frac{K_{ECW} \cdot H^2 \cdot L_{seg,i}^2}{\text{real}[Z(10\text{KHz})]}$$

wobei H die Höhe des Körpers in cm, K_{TBW} eine Konstante der Proportionalität für das gesamte Wasser (TBW) und K_{ECW} eine Konstante der Proportionalität für das extrazelluläre Wasser ist, $k_{O_{TBW_{seg,i}}}$ für Segment i, $k_{O_{ECW_{seg,i}}}$ für das extrazelluläre Wasser (ECW) für Segment i die unabhängigen Terme, $L_{seg,i}$ und $L'_{seg,i}$ geometrische Terme sind, die für jedes Seg-

ment i bestimmt werden; entsprechend des Realwertes $[Z(\infty)]$ zu dem realen Wert bei einer Impedanz von über 100 kHz und unter 1 MHz für das Segment i , aber vorzugsweise bei R_0 , und dem Realwert $[Z(10 \text{ kHz})]$ des realen Wertes bei einer Impedanz über 10 kHz und unter 50 kHz für Segment i , aber vorzugsweise bei R_0 ;

c) der intrazelluläre Wassergehalt des Segmentes i , der mittels der Subtraktion $ECW_{seg, i}$ von $TBW_{seg, i}$ bestimmt wird,

d) das Gesamtvolumen und extrazelluläre Wasservolumen im Gesamtbereich, die durch die Summe der einzelnen Werte der Segmente i bestimmt werden sollen;

e) der Gehalt der fettfreien Masse im Segment oder der fettfreien Masse im Bereich $MM_{seg, i}$ und der globalen fettfreien Masse, mittels der Gleichung

$$MM_{seg, i} = \text{fettfreie Masse} = N + M \cdot \frac{D_{eq, seg, i}^2}{R(AF)}$$

wobei N und M die Terme sind, die von der linearen Rückentwicklung eingeführt werden, zwischen dem Verhältnis von:

$$\frac{D_{seg, i}^2}{Re[Z(\infty)]}$$

und der Wert der Menge an fettfreier Masse, gemessen mittels einer alternativen Methode, und die von der Art der menschlichen Rasse abhängt, und $D_{eq, seg, i}^2$ einem geometrischen Parameter von Segment i , wodurch der Globalwert der Menge an fettfreier Masse durch die Summe aller Werte $MM_{seg, i}$ und der globalen Fettmasse aus der Differenz zwischen dem Gewicht des untersuchten menschlichen Körpers und dem Gewicht der Menge an globaler fettfreier Masse, erhalten wird.

2. Verfahren nach Anspruch 1, **dadurch gekennzeichnet, dass** das gesamte und extrazelluläre Wasservolumen im Gesamtbereich durch Verwendung der RSI (Recht Hand Impedanz) bestimmt wird, so als ob es ein Segment wäre, wobei vorteilhaft die spezifischen Parameter der TBW und ECW Formeln berücksichtigt werden.

3. Vorrichtung zum Messen der elektrischen Impedanz bei verschiedenen Frequenzen zur Ausführung des Verfahrens nach den vorhergehenden Ansprüchen, **dadurch gekennzeichnet, dass** es sich

aus einer Hauptplatine (15) zusammensetzt, die verbunden ist mit: einer elektrischen Quelle (20); einer Signalgeneratorkarte (16), die mindestens zwei gewählte Frequenzen als auch Referenzsignale für die Demodulation erzeugt; einer Karte zur Patientenschnittstelle (17), die die erzeugten Spannungssignale in Strom umwandelt; einer Signalerfassungskarte (18), die sich aus einem Differentialverstärker und einem Operationsverstärker (gain amplifier), mit über Software auswählbaren Verstärkungsgewinnen, zusammensetzt; einer A/D Empfangskarte (19), die mit einem A/D Umwandler von 16 Bit zur Abtastung für Datenempfang ausgestattet ist; wobei die Stromquelle (20) mit dem zu untersuchenden Körper über ein Multiplexgerät verbunden ist, das den Anschluss eines jeden Elektrodenpaares an die Quelle ermöglicht, die jede einzelne Elektrode mit einem Eingangspuffer verbindet, während jeder einzelne ihrer Ausgänge mit einem Multiplex-Schaltkreis verbunden ist, der in einen Differentialverstärker läuft und zwar über abgeschirmte Koaxialkabel; wobei die Steuerung des Systems über einen Mikroprozessor geführt wird.

4. Vorrichtung nach Anspruch 3, **dadurch gekennzeichnet, dass** sie mit einem Beschleunigungsmesser versehen ist, der die Beschleunigungsmessung durchführt, mit der der Körper untersucht wurde, und zwar auf eine synchrone Art und Weise mit der Impedanzmessung.

Revendications

1. Procédure pour mesurer les volumes et la composition corporelle globale et segmentaire chez des êtres humains, en mesurant l'impédance électrique à des fréquences différentes, au moins quatre, comprises dans l'intervalle de 1 kHz à 1 MHz, dans laquelle une première estimation du rapport entre les volumes d'eau total et d'eau extracellulaire est obtenue au moyen du quotient k entre le module d'impédance à basse fréquence $Z(BF)$, située entre 1 kHz et 50 kHz, et le module d'impédance à haute fréquence $Z(AF)$, située entre 100 kHz et 10 MHz, ladite valeur k étant indépendante des conditions du contour de mesure, **caractérisée en ce qu'un** ajustement est effectué aux points expérimentaux par la méthode des moindres carrés, à la fois au niveau global et segmentaire, au moyen de l'expression de l'impédance électrique (Z) suivante, basée sur la fréquence (f):

$$Z(f) = R_0 + \frac{R_0 - R_\infty}{1 - \left(\frac{f}{f_c}\right)^{1-\alpha}}$$

déterminant ainsi les valeurs R_∞ , R_0 , f_c et α , qui représentent respectivement la résistance à une fréquence infinie, la résistance à la fréquence zéro, la fréquence à laquelle $\text{Im}(Z)$ est maximum et la dispersion des cellules du systèmes biologique, avec lesquelles les valeurs suivantes sont calculées :

a) le rapport entre le volume d'eau intracellulaire et le volume d'eau extracellulaire, donné par l'équation :

$$E = \frac{R_0 - R_\infty}{R_\infty}$$

b) la teneur totale en eau d'un segment i ($\text{TBW}_{\text{seg},i}$), donnée par l'équation :

$$\text{TBW}_{\text{seg},i} = \text{KO}_{\text{TBW}_{\text{seg},i}} + \frac{K_{\text{TBW}} \cdot H^2 \cdot L_{\text{seg},i}^2}{\text{Rea}[Z(\infty)]}$$

et la teneur d'un segment i en eau extracellulaire ($\text{ECW}_{\text{seg},i}$), qui est déterminée par :

$$\text{ECW}_{\text{seg},i} = \text{KO}_{\text{ECW}_{\text{seg},i}} + \frac{K_{\text{ECW}} \cdot H^2 \cdot L_{\text{seg},i}^2}{\text{rea}[Z(10\text{KHz})]}$$

H étant la hauteur du corps en cm, K_{TBW} une constante de proportionnalité pour l'eau totale (TBW) et K_{ECW} une constante de proportionnalité pour l'eau extracellulaire, $\text{KO}_{\text{TBW}_{\text{seg},i}}$ le terme indépendant pour le segment i, $\text{KO}_{\text{ECW}_{\text{seg},i}}$ pour l'eau extracellulaire (ECW) du segment i, $L_{\text{seg},i}$ et $L'_{\text{seg},i}$ sont des termes géométriques à déterminer pour chaque segment i ; en faisant correspondre la valeur réelle $[Z(\infty)]$ à la valeur réelle d'une impédance supérieure à 100 kHz et inférieure à 1 MHz pour le segment i, mais de préférence à R_∞ , et la valeur réelle $[Z(10\text{kHz})]$ à la valeur réelle d'une impédance supérieure à 10 kHz et inférieure à 50 kHz pour le segment i mais de préférence à R_0 ;

c) la teneur du segment i en eau intracellulaire qui est déterminée en soustrayant $\text{ECW}_{\text{seg},i}$ de $\text{TBW}_{\text{seg},i}$;

d) le volume d'eau total et le volume d'eau extracellulaire au niveau global qui seront déterminés par la somme des valeurs respectives des segments i ;

e) la teneur de la masse maigre segmentaire ou régionale $\text{MM}_{\text{seg},i}$ et globale au moyen de l'équation :

$$\text{MM}_{\text{seg},i} = \text{Lean Mass} = N + M \cdot \frac{D_{\text{eq,seg},i}^2}{R(\text{AF})}$$

N et M étant des termes qui sont introduits d'après la régression linéaire entre le rapport :

$$\frac{D_{\text{seg},i}^2}{\text{Re}[Z(\infty)]}$$

et la valeur de la quantité de masse maigre mesurée au moyen d'une méthode alternative et qui dépend du type de race humaine, et de $D_{\text{eq,seg},i}^2$, un paramètre géométrique du segment i, en obtenant la valeur globale de la quantité de masse maigre d'après la somme de toutes les valeurs de $\text{MM}_{\text{seg},i}$ et la masse grasse globale d'après la différence entre le poids du corps humain étudié et le poids de la quantité globale de matière maigre.

2. Procédure selon la revendication 1, **caractérisée en ce que** le volume d'eau total et le volume d'eau extracellulaire au niveau global sont déterminés en utilisant le RSI (impédance du côté droit) comme s'il était un segment en considérant comme il convient les paramètres spécifiques des formules de TBW et ECW.
3. Appareil pour mesurer l'impédance électrique à diverses fréquences destiné à mettre en oeuvre la procédure selon l'une des revendications précédentes, **caractérisé en ce qu'il** consiste en un panneau arrière (15) qui relie : une source de courant électrique (20) ; une carte génératrice de signaux (16) qui génère au moins deux fréquences choisies ainsi que des signaux de référence pour la démodulation ; une carte d'interface patient (17) qui convertit les signaux de tension générés en courant, une carte détectrice de signaux (18) qui est constituée d'un amplificateur différentiel et d'un amplificateur de gain ayant des degrés d'amplification sélectionnés par voie logicielle ; une carte d'acquisition A/N (19) qui est pourvue d'un convertisseur A/N de 16 bits afin d'échantillonner l'acquisition des données ; la source de courant (20) étant connectée au corps à l'étude au moyen d'un multiplexeur qui permet de connecter n'importe quelle paire d'électrodes à ladite source, connectant chacune des électrodes à une mémoire tampon d'entrée, alors que chacune de leurs sorties est connectée à un circuit multiplexeur qui alimente un amplificateur différentiel, au moyen de câbles coaxiaux blindés ; le contrôle du système étant réalisé au moyen d'un microcontrôleur.

4. Appareil selon la revendication 3, **caractérisé en ce qu'**il est pourvu d'un accéléromètre qui fournit la mesure de l'accélération auquel le corps a été soumis, d'une manière synchronisée avec la mesure de l'impédance.

5

10

15

20

25

30

35

40

45

50

55

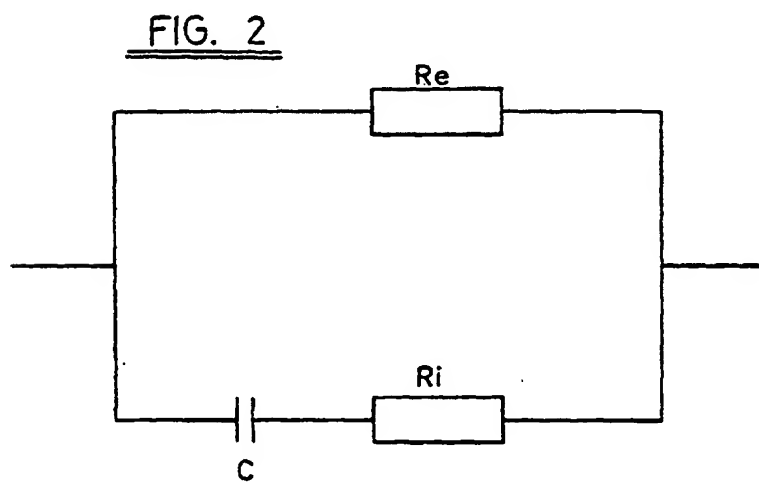
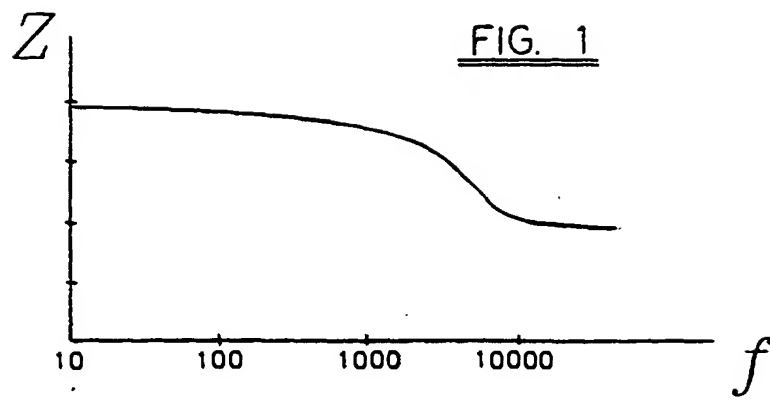


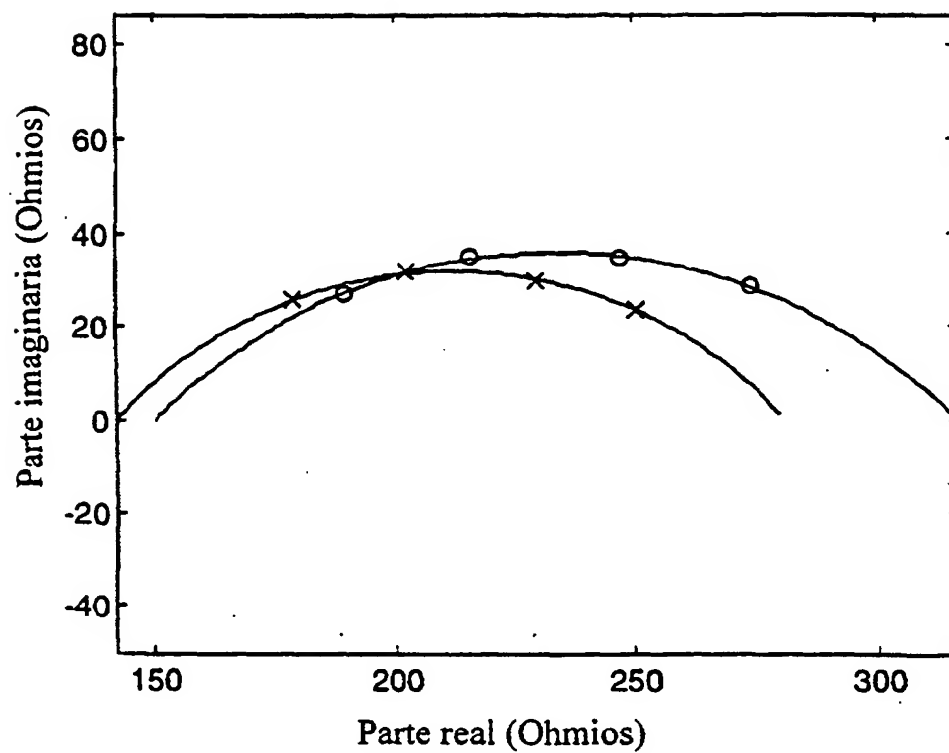
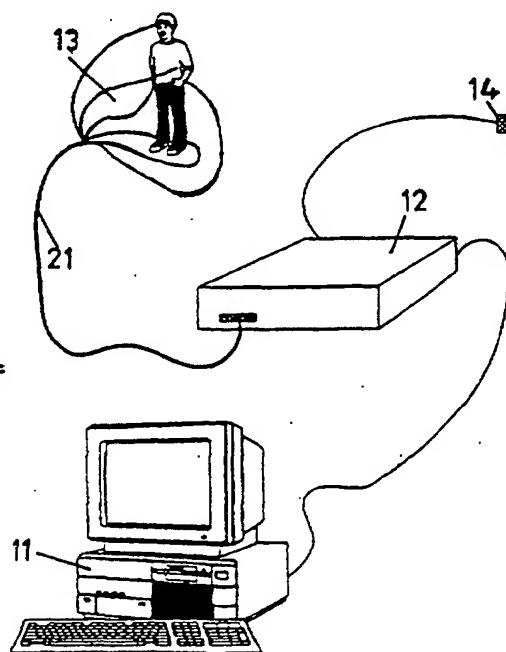
FIG. 3FIG. 4

FIG. 5

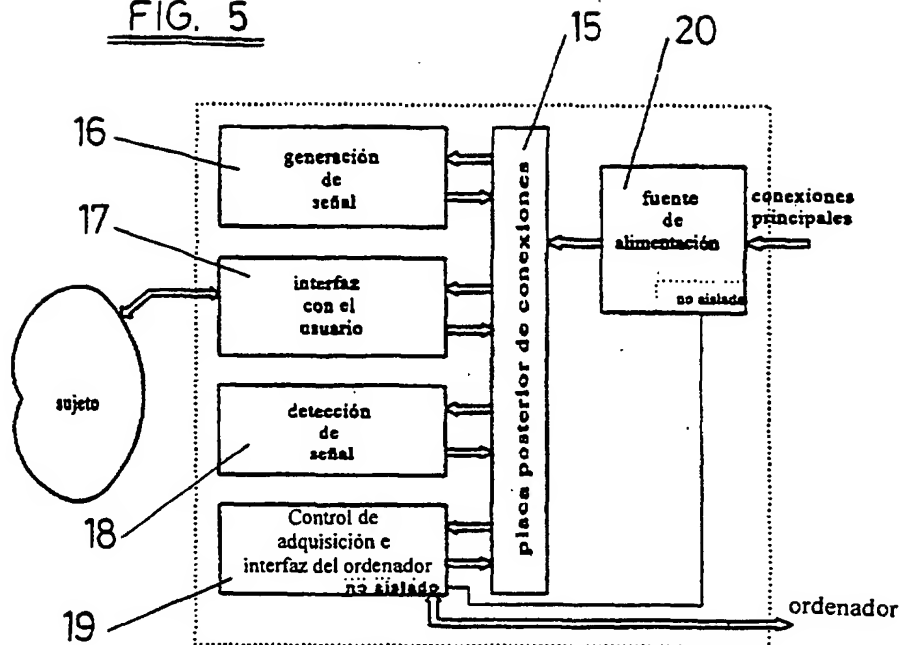


FIG. 6

